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Gene therapy could cure diabetes

Barcelona (dpa) - Gene therapy may provide a cure for diabetes, Spanish press reports said Wednesday.

Researchers at the Autonomous University of Barcelona have cured diabetes of the type 1 in mice, which had been genetically programmed to have the disease.

The scientists introduced into mouse embryos a gene known as IGF-1, which allows the pancreas to regenerate cells producing insulin.

Diabetes of the type 1 is the most serious form of the disease, in which the pancreas secretes insufficient insulin and the body in consequence fails to metabolize glucose.

Symptoms range from constant hunger to blurred vision and extreme fatigue. The patient needs daily injections of insulin. Untreated, the disease can cause the patient to lapse into a life-threatening diabetic coma.

Team leader Fatima Bosch warned that the results were preliminary and that it would take years before they could be tested on humans.

The research was published in the Journal of Clinical Investigation.

dpa

Deutsche Presse-Agentur (dpa)

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Nation

Posted on Mon, Sep. 09, 2002

Gene therapy project cures dogs of rare disease

BY TINA HESMAN
St. Louis Post-Dispatch

ST. LOUIS - (KRT) - Scientists from Washington University and the University of Pennsylvania have used gene therapy in dogs to cure a rare genetic disease that affects multiple body organs.

The researchers, led by Katherine Parker Ponder at Washington University and Mark E. Haskins of the University of Pennsylvania, used gene therapy to treat seven dogs with a disorder known as MPS VII. In humans, the disease is called Sly syndrome - named for Dr. William Sly, a doctor at St. Louis University who first diagnosed the disease in 1973.

Other researchers have used gene therapy in dogs to target diseases that affect a single body function, such as vision or blood clotting, but the 17-month study published Tuesday in the Proceedings of the National Academy of Sciences is the first to report successful treatment for a disease that affects many different organs, Haskins said.

Sly syndrome is a disease caused by a lack of the enzyme beta-glucuronidase. Without the enzyme, the body can not break down certain sugar molecules, causing the sugars to build up in storage compartments, called lysosomes, within cells. Overstuffing the storage compartments damages cells and leads to defects in almost every organ system in the body, especially the bones, eyes, heart valves and liver. People with the disease have stunted growth, mental retardation and trouble moving. They usually die in childhood. The disease affects about one in 27,000 babies born in the United States.

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Although rare, the disease is a good model for treating other storage diseases, such as Tay-Sachs disease, Sly said.

Ponder and other colleagues first used gene therapy to treat mice with the MPS VII disease. The researchers then turned to the dogs to see if such therapies might be useful to treat people.

"We were interested in a large animal model because it's getting to the point where anybody can cure a mouse," Ponder said. But researchers have rarely been able to use the rodent cures to treat larger animals or people, she said.

Ponder and her co-workers replaced genes in a retrovirus with a healthy copy of the gene for the beta-glucuronidase enzyme.

The scientists then injected newborn puppies affected with the MPS VII disease with the engineered retrovirus. The scientists later found liver cells in the dogs producing the beta-glucuronidase enzyme, proof that the gene therapy had worked. The liver cells made enough of the enzyme to correct the disease throughout the body.

The puppies gained weight almost normally and were able to walk and run. The dogs didn't develop the serious heart and eye problems normally found in dogs with the disease.

The technique could be used to cure many other lysosomal storage diseases, which affect about one of every 7,000 babies born, Sly said. It also may be useful in developing gene therapy for other enzyme deficiencies.

The therapy could be ready for human use in five to 10 years, Ponder predicted.


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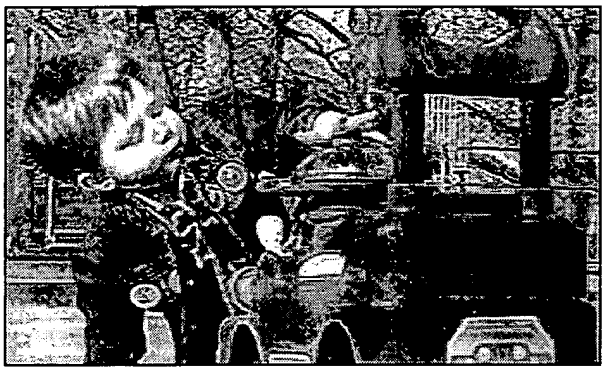
EXHIBIT A 6-11

Wednesday, 3 April, 2002, 12:24 GMT 13:24 UK

'Bubble boy' saved by gene therapy



Rhys can now play outside

In one of the first treatments of its kind, UK doctors have used gene therapy to cure a toddler of a potentially fatal disorder.

Scientists at Great Ormond Street Hospital in London successfully treated 18-month-old Rhys Evans, who had a condition preventing him from developing an immune system.

The problem, called severe combined immunodeficiency (SCID) is caused by a single mutated gene, and meant that he had to live in sterile conditions or risk picking up a life-threatening infection.

Rhys, from Treharris, nr Cardiff, had spent much of his life in hospital prior to the treatment.

Only one in between 50,000 and 100,000 births in the UK is affected by the disorder.

66 **After his gene therapy, he was running around at home - he's a normal little boy now** 99

Dr Adrian Thrasher, Great Ormond Street Hospital

However, following the ground-breaking treatment, which adds in a correctly-functioning version of the faulty gene, it is hoped that he will be able to lead a normal

WATCH/LISTEN ON THIS STORY

- **The BBC's Karen Allen**
  "He was born without an immune system"
- **Rhys Evans' consultant Dr Adrian Thrasher**
  "We know what the genetic defect in his bone marrow is"
- **Professor Christine Kinnon, Great Ormond Street**
  "There are other immune diseases which will be applicable to this treatment"

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life.

And doctors are hopeful that children with other similar genetic disorders could benefit in a similar way.

Gene therapy for SCID - often dubbed the "baby in a bubble" syndrome - has only been successful in two other cases, treated at a Paris Hospital in 2000.

Gene therapy hurdles

In general, attempts to use gene therapy in a wide variety of medical fields have had only limited success so far.

This is because it has proved difficult to get the therapy to the cells which need it.

However, the Great Ormond Street team, led by Dr Adrian Thrasher, is now moving on to tackle other similar disorders caused by a single gene defect.

Dr Thrasher told the BBC: "We're very excited by this - he was incredibly sick, with a nasty pneumonia, a life threatening infection.

"After his gene therapy, he was running around at home - he's a normal little boy now."

66 **Since they cracked the genetic code and found the gene, they can work miracles** 99

Marie Evans, Rhys' mother

Rhys' mother Marie said that she had been restricted to fortnightly visits because Rhys had to stay at Great Ormond Street while she returned home.

She said: "It is difficult to look at what we have been through - we see him now, playing with other children, and it's just amazing.

"Since they cracked the genetic code and

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Links to more Health stories are at the foot of the page.

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found the gene, they can work miracles."

Rhys needed to be kept in a sterile environment (home video pictures)

No donor

The only existing treatment for SCIDs is bone marrow transplantation, but in the case of Rhys, a matching donor could not be found.

Instead, Dr Thrasher's team took bone marrow from the boy, then used a virus to carry a new version of the gene into immune cells from the marrow.

This was then reimplanted into the patient, where it gradually began to generate further cells to pass into the bloodstream and protect him from infection.

Now he has a normal count of immune cells for a child of his age, and doctors are hopeful this will continue.

This particular type of SCID, called "X-linked" SCID, affects only boys.

The scientists now want to try to correct an illness called chronic granulamatous disorder (CGD), which again invovles a single defective gene.

The success is the first for the newly-launched gene therapy laboratory at Great Ormond Street, which was partly funded by the trust's "Jeans for Genes" appeal.

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EXHIBIT A
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Date: 3 April 2002

Gene therapy cures life threatening disease at Great Ormond Street Hospital: Successful 'first' funded by Jeans for Genes

A child has been cured of a fatal genetic condition, X-SCID, by gene therapy at Great Ormond Street Hospital. This is the first time gene therapy has cured a child in Britain.

The success, which follows the opening of the gene therapy laboratory at Great Ormond Street last September, is one of the few clinically successful examples of gene therapy anywhere in the world.

The trials were a joint venture between Great Ormond Street Hospital and the Institute of Child Health, and were funded with proceeds from the Jeans for Genes Campaign.

The Jeans for Genes campaign is now in its seventh year and was set up to raise funds for research into genetic diseases. The gene therapy cure is the first substantial clinical result from this work.

What is X-SCID?

X-SCID is x-linked Severe Combined Immunodeficiency Disease. A fuller brief on the condition is available. The child is born with no immune system of their own and becomes highly vulnerable to infection as they lose maternal immunity.

Contact Information:
Stephen Cox
GOS-ICH Press Office 020 7829 8671
Email: Coxs@gosh.nhs.uk
Out of hours page via switchboard 020 7405 9200

Liz Ivens
Jeans for Genes Press Office 020 7813 8103

Further information available:
Information for parents
The facts: Gene therapy at Great Ormond Street
The future of gene therapy at GOSH: Information for concerned parents

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Useful links:

www.bbc.co.uk/genes
Excellent BBC site packed with useful bits on genes and history, tricky ethical issues and cloning. Great animation for children.

www.cafamily.org.uk
UK charity providing support and advice to parents of children with a wide range of medical conditions.

www.ukfgi.org.uk
Insurance issues for people with genetic conditions.

www.geneticalliance.org
International organisation supporting sufferers of a wide range of genetic disorder.

www.yourgenome.org
Handy beginners' guide to genetics with latest news and discussion forum.

www.becominghuman.org
Interactive documentary telling the story of human evolution.

vector.cshl.org
History of genetics and DNA from the beginning with some delightful animation, plus audio and video interviews.

www.ornl.gov/hgmis
US government portal site on the human genome project.

gdbwww.gdb.org/gdb
A search tool to explore the genome database.

Notes to editors:

Great Ormond Street Hospital for Children NHS Trust, Great Ormond Street, London WC1N 3JH
Tel: +44 (0)20 7405 9200, Fax: +44 (0)20 7829 8643
and The Institute of Child Health, 30 Guilford Street, London WCIN 1EH
Tel: +44 (0)20 7242 9789, Fax: +44 (0)20 7831 0488
Contact us